Applicant also presents some amendments to the claims and respectfully requests their entry.

Applicant has also filed a petition for an extension of time to the present date with payment of the appropriate fee.

AMENDMENTS

IN THE CLAIMS:

Please cancel claims 98, 100, 101, 105, 110, 115, 117-119, and 130 without prejudice.

Please amend claims 78-81, 91 and 123 as follows:

78. (AMENDED) A method for preparing a protein having a correctly folded human insulin precursor comprising:

expressing a recombinant protein comprising, from N-terminus to C-terminus, a first peptidyl fragment which has an amino acid sequence which is at least 60% identical to a sequence of SEQ ID NO: 1 of the same length as the first fragment, a second peptidyl fragment which is a human insulin precursor, and at least one cleavable peptidyl fragment linking the first and second peptidyl fragments, wherein the first peptidyl fragment is capable of increasing the yield of the bioactive conformation of the insulin precursor formed upon contact of the recombinant protein with a chaotropic auxiliary agent as compared to the yield of the bioactive conformation of the insulin precursor formed from contacting the same recombinant protein lacking the first peptidyl fragment with the chaotropic agent;

contacting the recombinant protein with an aqueous medium comprising the chaotropic agent; and

whereby the protein is correctly folded.

79. (AMENDED) A method according to claim 78, wherein the aqueous medium comprises at least one chaotropic auxiliary agent.

80. (AMENDED) A method according to claim 78, wherein one of the at least one chaotropic auxiliary agent is urea.

81. (AMENDED) A method according to claim 80 wherein the urea is present in a concentration between about 2 M and 8 M.

91. (AMENDED) A method according to claim 78, wherein the recombinant protein is contacted with a mercaptan.

123. (AMENDED) A chimeric protein comprising from N-terminus to C-terminus:

a first peptidyl fragment which comprises an amino acid sequence at least 60% identical to the first 20 N-terminal amino acids of SEQ ID NO: 1;

a second peptidyl fragment comprising a human insulin precursor which exhibits insulin-like bioactivity when folded in a bioactive conformation; and

at least one cleavable peptidyl fragment linking the first and second peptidyl fragments;

wherein the first peptidyl fragment mediates folding of the second peptidyl fragment to cause the second peptidyl fragment to adopt the bioactive conformation.

Please add the following new claim:

--131. (NEW) A method of making a correctly folded human polypeptide with insulin bioactivity, said method comprising:

expressing a recombinant protein comprising, from N-terminus to C-terminus, a first peptidyl fragment which has an amino acid sequence which is at least 60% identical to a sequence of SEQ ID NO: 1 of the same length as the first fragment, a second peptidyl fragment which is a human insulin precursor, and at least one cleavable peptidyl fragment linking the first and second peptidyl fragments, wherein the first peptidyl fragment is capable of increasing the yield of the bioactive conformation of the insulin precursor formed upon contact of the protein with a chaotropic auxiliary agent as